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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/068,528	05/13/1998	SATOSHI KOIZUMI	766.20	2408

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[REDACTED] EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	36

DATE MAILED: 11/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/068,528	KOIZUMI ET AL.
	Examiner	Art Unit
	Manjunath N. Rao, Ph.D.	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 02 October 2002.
- 2a) This action is **FINAL**.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1,5,15,16,18-20 and 72 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1,5,15,16,18-20 and 72 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)                  4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)                  5) Notice of Informal Patent Application (PTO-152)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.                  6) Other: \_\_\_\_\_ .

**DETAILED ACTION**

Claims 1, 5, 15, 16, 18-20 and 72 are still at issue and are present for examination. Examiner regrets the inadvertent error in reciting the pending claims in the previous Office action. Examiner also brings the attention of the applicant that claim 19 is still under consideration as opposed to the applicants remark that it has been cancelled or that it is no longer under consideration (see page 3, under "Remarks" of response filed on August 19, 2002).

Applicants' amendments and arguments filed on 8-19-02 and 9-25-02, paper No.33 and 35, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

*Specification*

The amendment filed on 9-25-02 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Claim 1 is now directed specifically for a process producing a sugar nucleotide comprising selecting as enzyme sources a) a culture broth of a microorganism capable of producing GTP or UTP from a nucleotide precursor. The same claim was previously directed to an enzyme source in a) as a microorganism capable of producing NTP from a nucleotide precursor. Examiner was unable to find support for specific use of a culture broth of

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a microorganism capable of producing GTP or UTP from a nucleotide precursor as an enzyme source. Therefore the above recitation is considered as new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5, 15, 16, 18-20 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akihiko et al. (EP 0553821A1, 4-8-93), Zapata et al. (J. Biol. Chem. Vol. 264(25):14769-14774) and the common knowledge in the art that CMP-NeuAc can be synthesized from CTP and NeuAc (Biochemistry, 3<sup>rd</sup> Ed, 1988, by Stryer). Claims 1, 5, 15, 16, 18-20 and 72 are drawn to a method of synthesizing a sugar -nucleotide such as CMP-sialic acid by combining a) culture broth, supernatant etc. of a microorganism (such as *C.ammoniagenes*) capable of producing an NTP such as GTP or UTP from a nucleotide precursor; b)a culture broth, culture supernatant etc. of a microorganism (such as *E.coli* or *C.ammoniagenes*) having genes responsible for production of sugar-nucleotide such as GDP or UDP from a sugar selected from a group consisting of glucose, fructose, galactose, sialic acid etc., allowing the enzyme sources the nucleotide precursor and the sugar to be present in an aqueous medium to form and accumulate the sugar-nucleotide and recover the same.

Akihiko et al. teach the synthesis of CTP-choline using orotic acid from two groups of microorganisms which they call as Microorganism A2 and microorganism B. While microorganism B (*C.ammoniagenes*) has the capability of converting orotic acid to UDP and or UTP (see page 3 of the reference), microorganism A2 (*E.coli*)has the capability of converting UTP to CTP and CTP-choline only in the presence of phosphorylcholine. However, it would be obvious to one of skill in the art that microorganism A2 will accumulate the CTP when phosphorylcholine is deleted from the reaction.

Zapata et al. teach the cloning of gene which is responsible for encoding sialic acid synthase which forms CMP-sialic acid in the presence of CTP and sialic acid. The reference provides a clone which expresses the gene by 10-30 folds in excess of what is produced by the wild type.

Therefore, it would have been obvious to one of ordinary skill in the art, especially those interested in developing a simple and cost-effective method of preparing CMP-sialic acid, by growing the Microorganism A2 and microorganism B of Akihiko et al. (which produces CTP starting from orotic acid) along with the clone of Zapata et al. in a medium comprising orotic acid and sialic acid to produce CMP-sialic acid. One of ordinary skill in the art would have been motivated to do as other methods to produce the same sugar-nucleotide is either cumbersome or not cost-effective. One of ordinary skill in the art would have a reasonable expectation of success since the reference of Akihiko et al. explicitly teach and provide the required microorganisms to produce CTP from a cheap substrate such as orotic acid and Zapata et al. provide a clone that can form CMP-sialic acid from sialic acid and CTP. Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office action, applicants have traversed the above rejection arguing that Akihiko et al. discloses a process for producing CTP-choline converting UTP or CTP but does not disclose or suggest any production using a GDP or UDP sugar as recited in the pending claims. Examiner respectfully disagrees. As opposed to applicant's argument, Akihiko et al. describe in detail all the steps involved in arriving at CTP starting from the nucleotide precursor orotic acid via UMP and UDP. Applicants also disclose in their specification that the UDP sugar can be prepared starting from orotic acid using a microorganism which has the ability to do so (see page 23-25). Applicants also argue that Zapata et al. disclose a process of producing CMP-sialic acid but does not disclose or suggest the production of GDP-sugar or UDP -sugar. Applicants are arguing that both the above references should teach all the limitations of their invention. Examiner has used the reference of Zapata et al. to show as to how one skilled in the art would use the synthetase enzyme for the final preparation of product such as CMP-sialic acid. Therefore the above invention continues to be *prima facie* obvious to one of ordinary skill in the art and hence the above rejection is maintained.

### ***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao whose telephone number is (703) 308-3934. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao. Ph.D.  
22 November, 2002.

*Rebecca E. Prouty*  
REBECCA E. PROUTY  
PRIMARY EXAMINER  
*RECEIVED  
NOV 26 2002  
1600*